MALARIA

Dr Nashwan Mansoor

Malaria

- **Malaria in humans is caused by:-**
  - ***Plasmodium falciparum. (most strong pathogenicity)***
  - ***P. vivax. (most common)***
  - ***P. ovale.***
  - ***P. malariae.***
  - ***P. knowlesi.***
- ***Each species has its own morphologic, biologic, pathogenic, and clinical characteristics.***

- **It is transmitted by the bite of infected female anopheline mosquitoes.**

Malaria

- **The WHO estimates that 214 million cases of clinical malaria occurred in 2015, 88% of these in Africa, especially among children and pregnant women.**

- ***P. falciparum* has now become resistant to chloroquine and sulfadoxine-pyrimethamine, initially in South-east Asia and now throughout Africa.**

- **Travelers are susceptible to malaria.**

Malaria

- Most cases are due to P. falciparum, usually from Africa.
- 1% die because of late diagnosis.
- Migrants from endemic countries who spend long periods of time in non-endemic countries.
- They have lost their partial immunity and frequently do not take malaria prophylaxis.

Malaria

❖ Modes of transmission :-

- **Principal mode of spread of malaria is by the bites of female anopheles mosquito.**
- **Blood transfusion (Transfusion malaria).**
- **Mother to the growing fetus (Congenital malaria).**
- **Needle stick injury : (Therapeutic inoculation of malarial parasites, so as to induce fever, was a mode of treatment for neurosyphilis).**

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Malaria

❖ **Pathogenesis :-**

➢ **Two hosts : female anopheles and humans.**

➢ **Two types of reproduction :-**

- **A sexual reproduction in human (Humans as intermediate host).**

- **Sexual reproduction in female anopheles (Female anopheles as final host).**

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❖ Pathogenesis :-

➢ Life cycle of the malarial parasite;-

- ✓ **The female anopheline mosquito becomes infected when it feeds on human blood containing gametocytes, the sexual forms of the malarial parasite.**

- ✓ **Development in the mosquito takes 7–20 days, and results in sporozoites accumulating in the salivary glands and being inoculated into the human blood stream.**

- ✓ **Sporozoites disappear from human blood within half an hour and enter the liver.**

Malaria

❖ Pathogenesis :-

➢ Life cycle of the malarial parasite;-

- ✓ **After some days, merozoites leave the liver and invade red blood cells, where further asexual cycles of multiplication take place, producing schizonts.**

- ✓ **Rupture of the schizont releases more merozoites into the blood and causes fever, the periodicity of which depends on the species of parasite.**

- ✓ **P. vivax and P. ovale may persist in liver cells as dormant forms, hypnozoites, capable of developing into merozoites months or years later.**

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Malaria

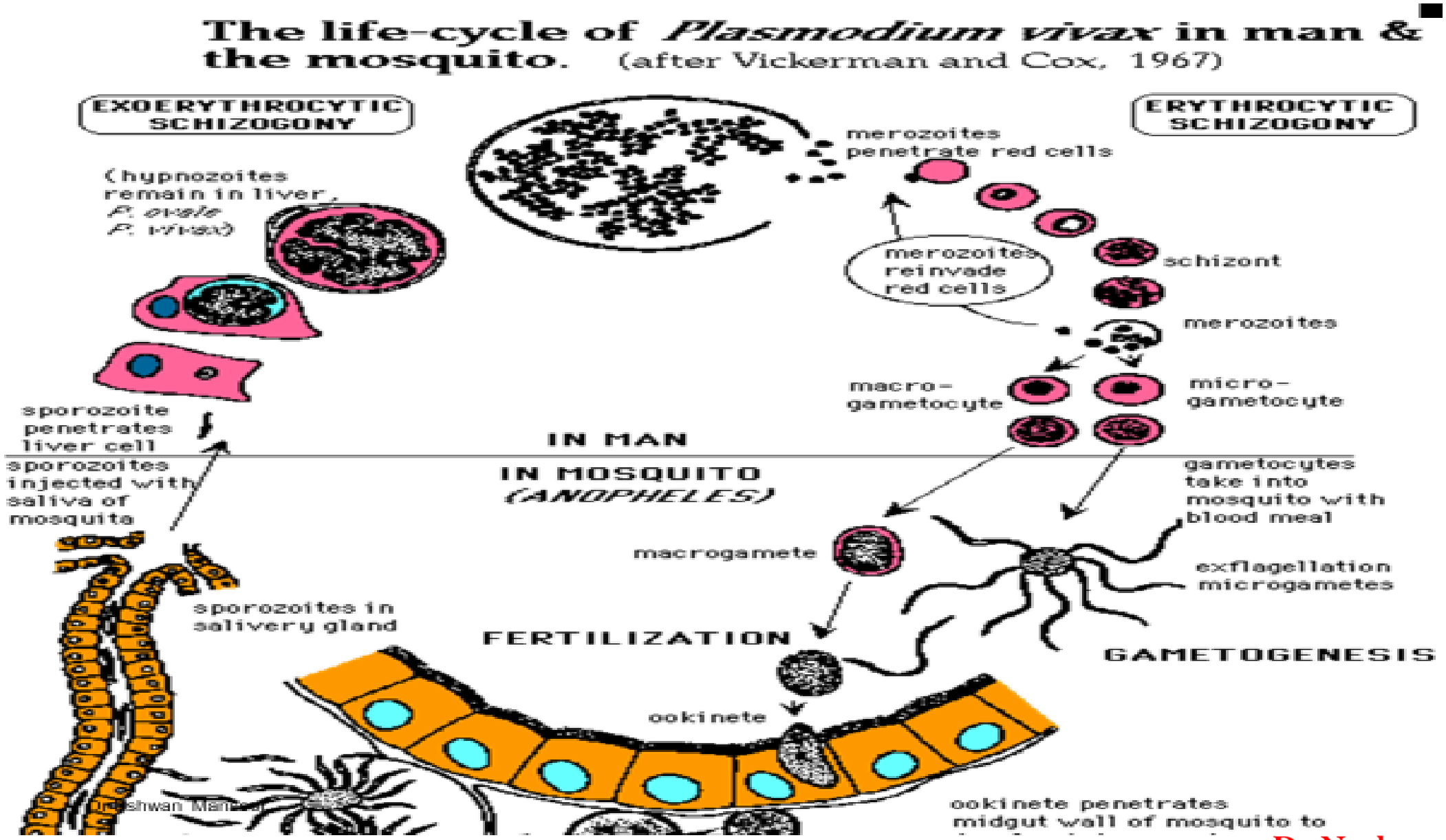
❖ Pathogenesis :-

➢ Life cycle of the malarial parasite;-

- ✓ **The first attack of clinical malaria may occur long after the patient has left the endemic area, and the disease may relapse after treatment with drugs that only kill the erythrocytic stage of the parasite.**

- ✓ **P. falciparum, P. knowlesi and P. malariae have no persistent exo-erythrocytic phase but recrudescence of fever may result from multiplication of parasites in red cells that have not been eliminated by treatment and immune processes.**

Malaria



Malaria

Malaria

❖ Pathology :-

- Red cells infected with malaria are prone to hemolysis.
- Is most severe with P. falciparum, which invades red cells of all ages.
- P. vivax and P. ovale and P. malariae invade young cells, so that infections remain lighter.
- Anaemia may be profound and is worsened by dyserythropoiesis, splenomegaly and depletion of folate stores.

Malaria

❖ Pathology :-

- In P. falciparum malaria, red cells containing trophozoites adhere to vascular endothelium in post-capillary venules in brain, kidney, liver, lungs and gut by the formation of ‘knob’ proteins.

- Also form ‘rosettes’ and rouleaux with uninfected red cells.

- Vessel congestion results in organ damage, which is exacerbated by rupture of schizonts, liberating toxic and antigenic substances.

- P. falciparum has influenced human evolution, with the appearance of protective mutations such as sickle-cell (HbS), thalassemia, glucose-6-phosphate dehydrogenase (G6PD) deficiency and HLA-B53.

Malaria

❖ Pathology :-

- P. falciparum does not grow well in red cells that contain hemoglobin F, C or especially S. Hemoglobin S heterozygotes (AS) are protected against the lethal complications of malaria.

- P. vivax cannot enter red cells that lack the Duffy blood group; therefore many West Africans and African Americans are protected.

Malaria

❖ Clinical features :-

- The clinical features of malaria are non-specific.
- The diagnosis must be suspected in anyone returning from an endemic area who has features of infection.
- In an endemic area , malaria often presents with atypical manifestations non specific flue-like symptoms (headache , fatigue ,myalgia, arthralgia, abdominal. pain, nausea, vomiting, hypotension).
- The patient age and immunity play a role in the severity of the presentation.

Malaria

❖ Clinical features :-

➢ Falciparum infection:-

- **Is the most dangerous of the malarias.**
- **The onset is often insidious, with malaise, headache and vomiting. Cough and mild diarrhoea are also common.**
- **The fever has no particular pattern. Jaundice is common due to hemolysis and hepatic dysfunction.**
- **The liver and spleen enlarge and may become tender.**

Malaria

- **Clinical features :-**
  - **P. falciparum infection:-**
    - **Anaemia develops rapidly, as does thrombocytopenia.**
    - **A patient with falciparum malaria, apparently not seriously ill, may rapidly develop dangerous complications.**
    - **Cerebral malaria is manifested by delirium, seizures or coma, usually without localizing signs.**
    - **Children die rapidly without any specific symptoms other than fever.**

Malaria

❖ Clinical features :-

➢ P. falciparum infection:-

- **Immunity is impaired in pregnancy and the parasite can preferentially bind to the placental protein chondroitin sulphate A.**
- **Abortion and intrauterine growth retardation from patriotization of the maternal side of the placenta are frequent.**
- **Previous splenectomy increases the risk of severe malaria.**

Malaria

❖ Clinical features :-

➢ P. vivax and P. ovale infection :-

- Mostly the illness starts with several days of continued fever before the development of classical bouts of fever on alternate days.
- Fever starts with a rigor.
- The patient feels cold and the temperature rises to about 40°C.
- After half an hour to an hour, the hot or flush phase begins.
- It lasts several hours and gives way to profuse perspiration and a gradual fall in temperature.

Malaria

❖ Clinical features :-

➢ P. vivax and P. ovale infection :-

- **The cycle is repeated 48 hours later.**
- **Gradually, the spleen and liver enlarge and may become tender.**
- **Anaemia develops slowly.**
- **Relapses are frequent in the first 2 years after leaving the malarious area and infection may be acquired from blood transfusion.**

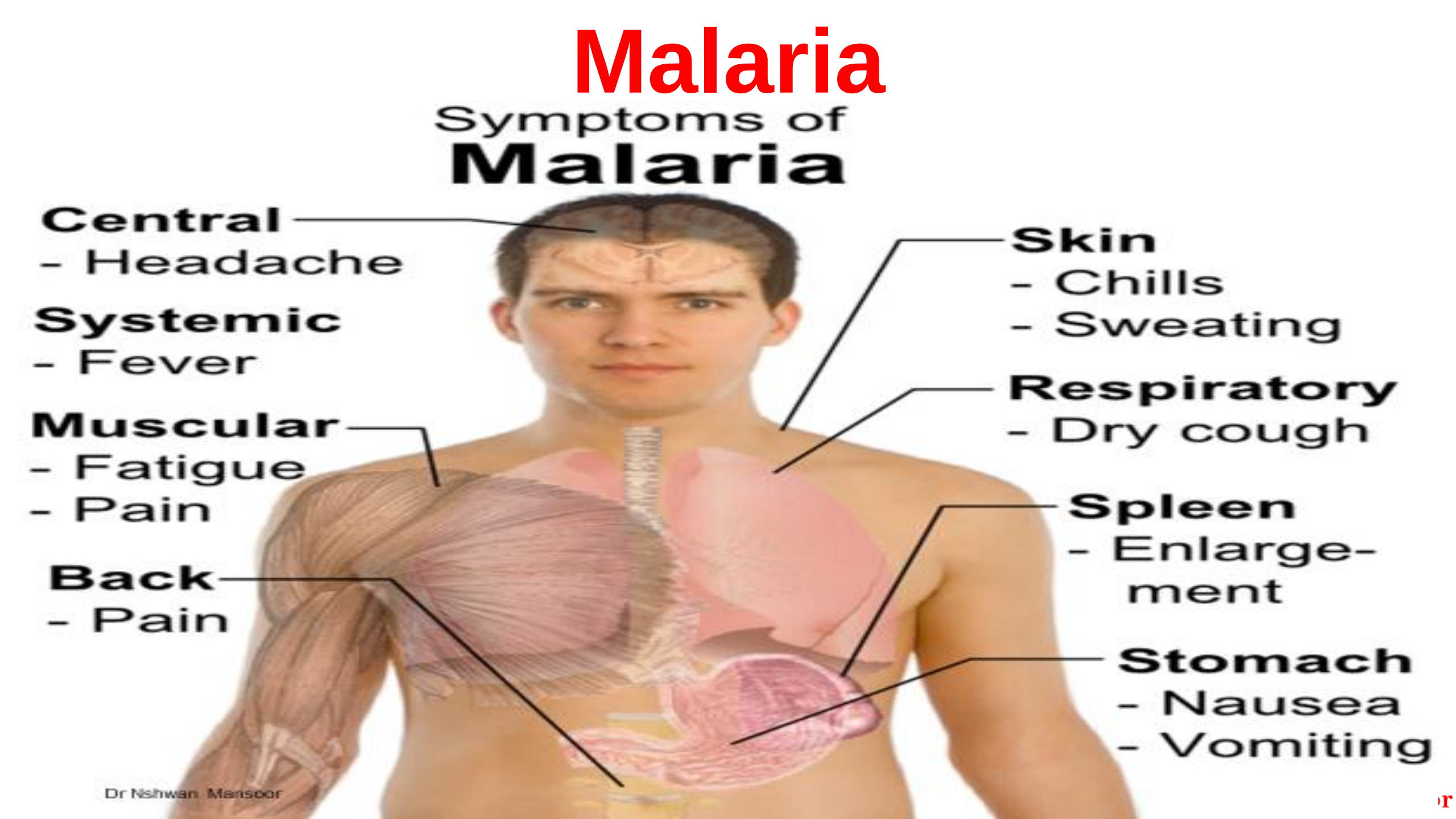
Malaria

❖ Clinical features :-

➢ P. malariae and P. knowlesi infection :-

- Usually associated with mild symptoms and bouts of fever every third day.
- Parasitemia may persist for many years, with the occasional recrudescence of fever or without producing any symptoms.
- Chronic P. malariae infection causes glomerulonephritis and long-term nephrotic syndrome in children.
- P. knowlesi is usually mild but can deteriorate rapidly.

Malaria


Symptoms of
Malaria
Central
- Headache
Systemic
- Fever
Muscular
- Fatigue
- Pain
Back
- Pain
Skin
- Chills
- Sweating
Respiratory
- Dry cough
Spleen
- Enlarge-
ment
Stomach
- Nausea
- Vomiting
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❖ **Sever malaria Complication:-**

- **Cerebral malaria Unarousable coma, Mortality around 20% .**
- **Convulsion >2 in 24hours.**
- **Metabolic acidosis:- due to;**

A) renal impairment.

B) Ketoacidosis.

C) lactic acidosis.

Malaria

❖ Sever malaria Complication:-

- **Renal failure: (with no improvement on rehydration).**
- **Pulmonary edema (ARDS).**
- **Hypotension: SBP<80mmhg DIC.**
- **Hemoglobinuria . (ATN).**

Malaria

❖ **Sever malaria Complication:-**

➢ **Severe anemia : Hb <5 , HCT<15 , parasitemia >100,000, due to;**

A) Destruction of RBC`s.

B) Ineffective erythropoiesis.

C) Spleen remove even normal RBC in severe form.

➢ **Hypoglycemia RBS<40 mg/dl. Due to;**

A) Gluconeogenesis.

B) Consumption by host and parasite.

C) by medication.

Malaria

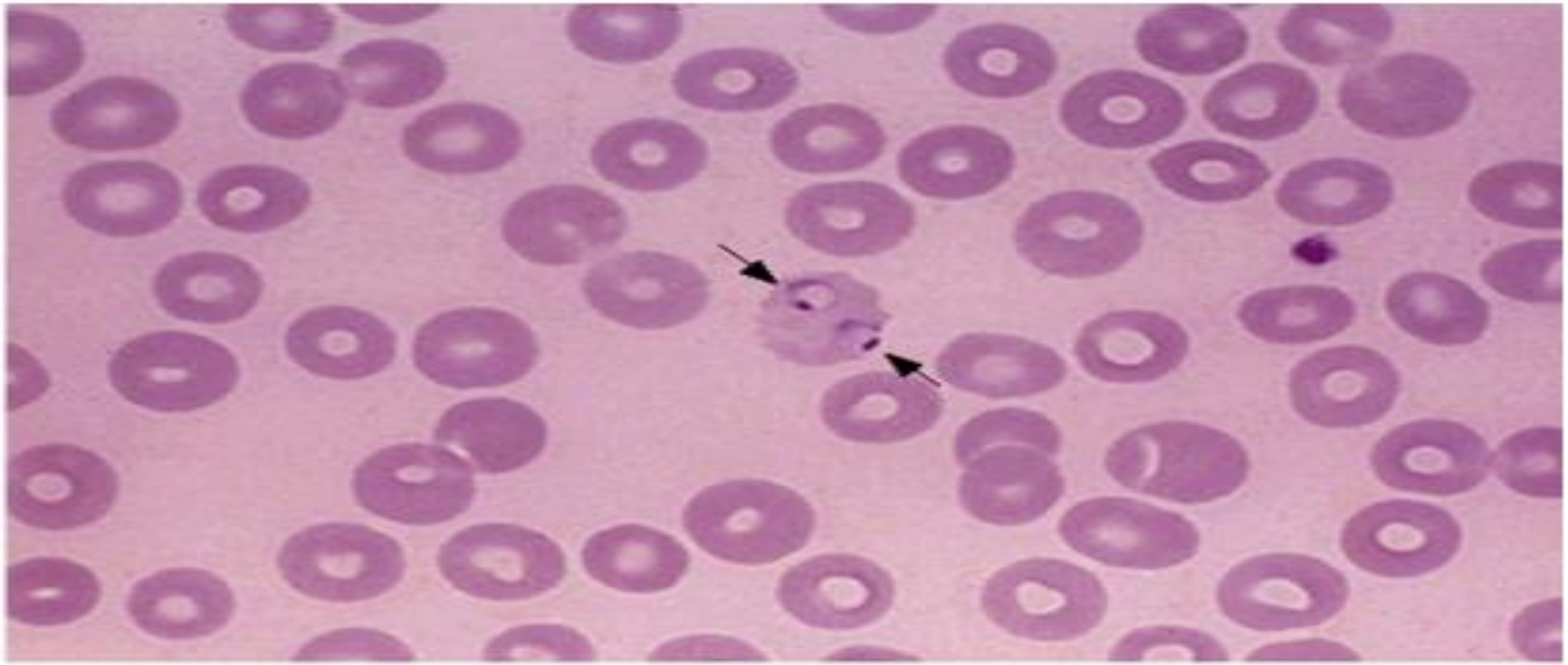
- **Investigations :-**
  - **MPS :- Definitive diagnosis.**
    - **To be done every 8 hours for 48 hours (Giems stain).**
    - **Giemsa-stained thick and thin blood films should be examined whenever malaria is suspected.**
    - **In the thick film, erythrocytes are lysed, releasing all blood stages of the parasite.**
    - **More blood is used in thick films, facilitates the diagnosis of low-level parasitemia.**
    - **A thin film is essential to confirm the diagnosis, species. and, in P. falciparum infections to quantify the parasite load .**

Malaria

- **Investigations :-**
- **MPS :- Definitive diagnosis.**
  - **In P. falciparum, only ring forms are normally seen in the early stages.**
  - **In the other species, all stages of the erythrocytic cycle may be found.**
  - **Gametocytes appear after about 2 weeks, persist after treatment and are harmless.**
  - **they are the source by which more mosquitoes become infected.**

Malaria

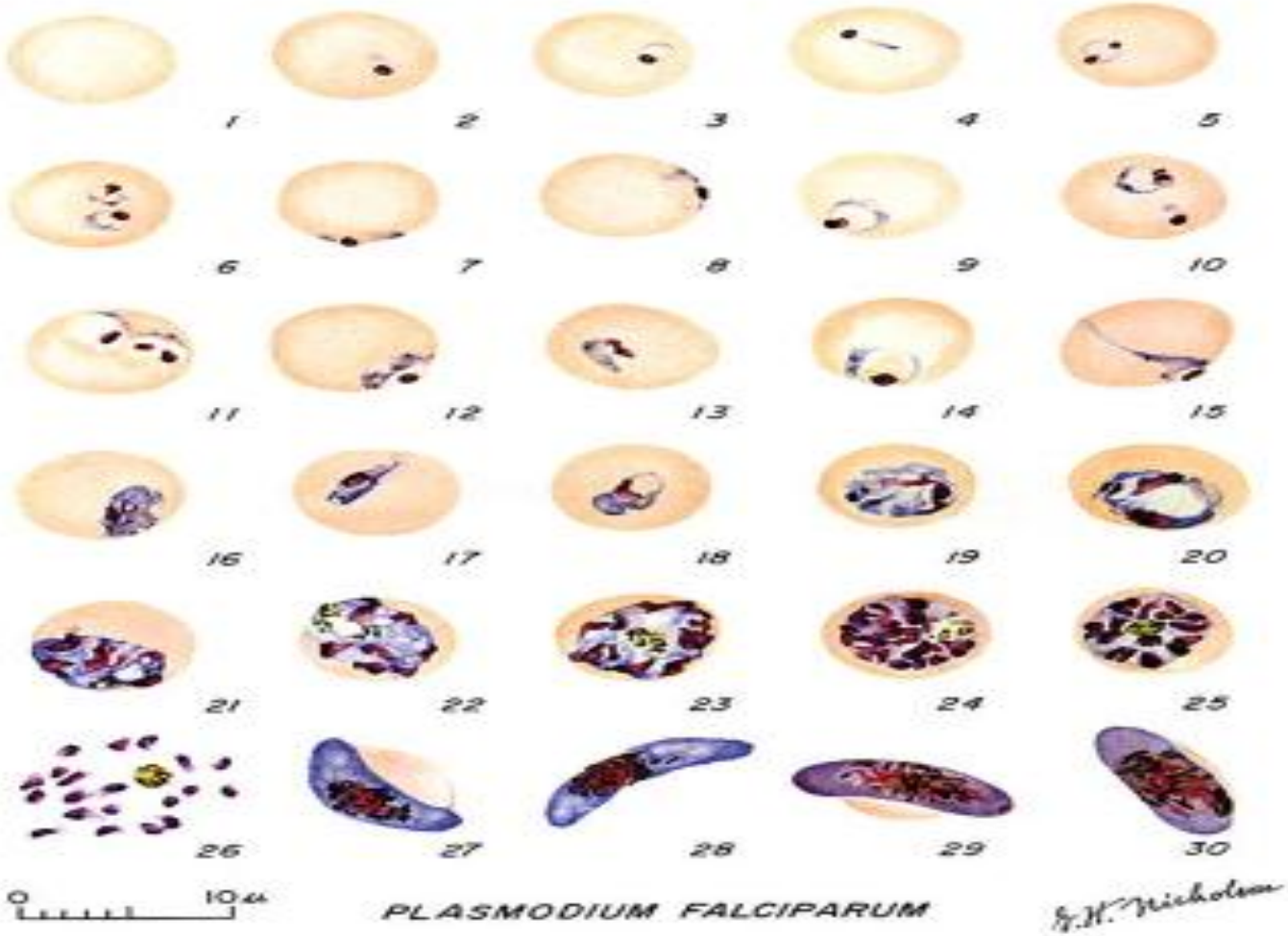
MALARIA – THICK SMEAR



Malaria Peripheral smear from a patient with malaria shows intraerythrocytic ring forms (trophozoites) (arrows). Courtesy of Carola von Kapff, SH (ASCP).

Malaria

Plasmodium falciparum: Blood Stage Parasites
Thin Blood Smears



1: Normal red cell

2-18: Trophozoites

(2-10: ring-stage trophozoites)

19-26: Schizonts (26 is a ruptured schizont)

27, 28: Mature macrogametocytes (female)

29, 30: Mature microgametocytes (male)

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Malaria

- **Investigations :-**
- **Immunochromatographic rapid diagnostic tests (RDTs):-**
  - **for malaria antigens.**
  - **Are extremely sensitive and specific for falciparum malaria but less so for other species.**
  - **Should be used in parallel with blood film examination but are especially useful where the microscopist is less experienced in examining blood films.**
  - **Are less sensitive for low-level parasitemia and positivity may persist for a month or more in some individuals.**

Malaria

- **Investigations :-**
- **DNA detection (PCR):-**
  - **Used mainly in research.**
  - **Useful for determining whether a patient has a recrudescence of the same malaria parasite or a reinfection with a new parasite.**

Malaria

❖ Investigations :-

➢ Other investigations:-

- **CBC : Hb : anemia.**
  PLT: decreased.
- **LDH: increased.**

- **G6PD screening for pt. before primaquine.**

Malaria

❖ **Differential diagnosis :-**

- **Septicemia.**
- **Leptospirosis.**

- **Typhoid fever .**
- **African trypanosomiasis.**

- **Babesiosis.**
- **Dengue fever.**

Malaria

❖ Management :-

A) Symptomatic and supportive treatment.

B) Etiologic treatment:

1) Control paroxysm treatment .

2) Prevent relapse.

3) Prevent transmission.

Malaria

❖ Management :-

A) Symptomatic and supportive treatment for;

- **High fever,**
- **Convulsion.**
- **Cerebral edema.**
- **Black water fever.**
- **Others.**

Malaria

❖ Management :-

B) Etiologic treatment:

1) Control paroxysm treatment .

➢ **Treatment should be guided by three main factors:**

1. The infecting Plasmodium species.

2. The clinical status of the patient.

3. The drug susceptibility of the infecting parasites as determined by the geographic area .

Malaria

❖ Management :- B) Etiologic treatment:

1) Control paroxysm treatment .

❑ Mild P. falciparum malaria:-

- ✓ **P. falciparum is now resistant to chloroquine and sulfadoxine-pyrimethamine (Fansidar) almost worldwide.**
- ✓ **An artemisinin-based treatment is recommended, e.g. co-artemether or artesunate–amodiaquine.**
- ✓ **A quinine is alternative treatment.**
- ✓ **Both treatment with or followed by doxycycline or clindamycin Atovaquone – proguanil.**

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Malaria

❖ Management :- B) Etiologic treatment:

1) Control paroxysm treatment .

❑ Complicated P. falciparum malaria:-

- ✓ **Severe malaria should be considered in any non-immune patient with:-**
  - **A parasite count greater than 2% or**
  - **With complications.**
- ✓ **Is a medical emergency.**

Malaria

❖ Management :- B) Etiologic treatment:

1) Control paroxysm treatment .

❑ **Complicated P. falciparum malaria:- Management includes:-**

- ✓ **Early and appropriate antimalarial chemotherapy.**
- ✓ **Active treatment of complications.**

- ✓ **Correction of fluid.**

- ✓ **Electrolyte and acid–base balance.**
- ✓ **Avoidance of harmful ancillary treatments.**

Malaria

❖ Management :- B) Etiologic treatment:

1) Control paroxysm treatment .

❑ Complicated P. falciparum malaria:-

- ✓ **The treatment of choice is intravenous artesunate.**
- ✓ **Rectal administration of artesunate is also being developed to allow administration in remote rural areas.**
- ✓ **Quinine salt is the alternative.**
- ✓ **Exchange transfusion may be beneficial for non-immune patients with persisting high parasitemia's (> 10% circulating erythrocytes).**

Malaria

❖ Management :- B) Etiologic treatment:

2) Prevent relapse :-

Late relapses can be prevented by used primaquine for 2 weeks.

Malaria

❖ Management :- B) Etiologic treatment:

3) Prevent transmission. :-

- **Clinical attacks of malaria may be preventable with chemoprophylaxis.**
- **Using chloroquine, atovaquone plus proguanil (Malarone), doxycycline or mefloquine.**
- **Gives the recommended doses for protection of the non-immune.**
- **The risk of malaria in the area to be visited and the degree of chloroquine resistance guide the recommendations for prophylaxis.**

Malaria

❖ Management :- B) Etiologic treatment:

3) Prevent transmission. :-

- Fansidar should not be used for chemoprophylaxis, as deaths have occurred from agranulocytosis or Stevens–Johnson syndrome.
- Mefloquine is useful in areas of multiple drug resistance.
- Experience shows it to be safe for at least 2 years but there are several contraindications to its use.
- Expert advice is required for individuals unable to tolerate the first-line agents listed or in whom they are contraindicated.
- Mefloquine should be started 2–3 weeks before travel to give time for assessment of side-effects.

Malaria

❖ Management :- B) Etiologic treatment:

3) Prevent transmission. :-

- Chloroquine should not be taken continuously as a prophylactic for more than 5 years without regular ophthalmic examination, as it may cause irreversible retinopathy.

- Pregnant and lactating women may take proguanil or chloroquine safely.

- Prevention also involves advice about the use of high percentage diethyltoluamide (DEET), covering up extremities when out after dark, and sleeping under permethrin-impregnated mosquito nets.

Good luck